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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/790,888	03/01/2004	Uri Wormser	85189-5800	2632

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EXAMINER	
BRADLEY, CHRISTINA	
ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 06/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/790,888	WORMSER, URI	
	Examiner	Art Unit	
	Christina Bradley	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *21 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *04/07/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Sequence Compliance

1. This application is objected to because the following amino acid sequences do not include a SEQ ID NO: page 12, line 30; page 13, lines 1, 2 and 6; page 18, lines 20 and 21; page 23, lines 24, 25, 26, 27, and 28; page 24, lines 23 and 24; and page 26, lines 16, 17, 18. All sequences longer than four amino acids referenced in the specification must include a SEQ ID NO and must be included in the Sequence Listing. See MPEP § 2421-2422.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

4. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or

chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

5. The instant application pertains to a skin extract with the ability to protect against inflammatory processes and noxious stimuli. The specification discloses an extract of burnt guinea pig skin that reduces the damage of thermal and mustard gas-induced burns. Although the specification identifies SEQ ID NOs:1-4 as the active ingredients in the extract, it does not provide evidence that other peptides or molecules are present. Despite this, claims 1, 3-5, 7, 8, and 14-26 are drawn to skin extracts comprising an unlimited number and type of active ingredients, claims 2, 6, 9, 11, 13, 27, and 29-33 are drawn to skin extracts comprising peptides, and claims 10, 12, 28, 34 and 35 are drawn to skin extracts comprising one or more peptides from the group consisting of SEQ ID NOs: 1, 2, 4-8 and 10-14. It is not clear from the specification if peptides of SEQ ID NOs: 5-8 and 10-14, their homologs, analogs and derivatives, or additional unidentified peptides or molecules are present in the extract obtained by the disclosed extraction procedure. Furthermore, despite the broad scope of the compounds and compositions claimed in this application, and the broad scope of diseases and conditions against which these compounds are claimed to effective, only a narrow set of compounds are described and possessed: a skin extract comprising at least one of SEQ ID NOs:1-4, and the isolated peptides SEQ ID NOs: 1-9, and 11-13. These compositions and compounds are only shown to be useful for protecting against thermal and mustard gas-induced burns. The critical chemical and structural features required for this or any other function are not fully elucidated in the specification. Accordingly, in

the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the skin extract or effective active components thereof commensurate with the broad scope of the claims.

6. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

7. With the exception of SEQ ID NOs:1-4, the skilled artisan cannot envision the detailed chemical structure of the skin extract useful for protecting against thermal and mustard gas-induced burns. With the exception of SEQ ID NOs: 1-9, and 11-13, the skilled artisan cannot envision the detailed chemical structure of isolated peptides that protect against thermal and mustard gas-induced burns. Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

8. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to

be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

9. Therefore, only a skin extract comprising at least one of SEQ ID NOs:1-4 as the active ingredient and the isolated peptides SEQ ID NOs: 1-9, and 11-13 useful for protecting against thermal and mustard gas-induced burns, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

10. Claims 1-35 are rejected under 35 U.S.C. 112, first paragraph because the specification while being enabling for a skin extract comprising at least one of SEQ ID NOs:1-4, and the isolated peptides SEQ ID NOs: 1-9, and 11-13, and their use in treating thermal and mustard gas –induced burns, does not reasonably provide enablement for all skin extract components and their use in treating all inflammatory processes and protecting against noxious stimuli. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The factors to be considered in determining whether the enablement requirement is met include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of

these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

11. In the instant case, claims 1-35 are drawn to a skin extract for protecting against inflammation and noxious stimuli, pharmaceutical compositions comprising the extract and methods of making and using thereof. The extract, which is obtained from guinea pig skin following a thermal burn and exposure to an iodine solution, has a protective effect against thermal and mustard gas-induced burns. The specification discloses that the active ingredients in the extract are four peptides, SEQ ID NOs: 1-4. Each of the four peptides in isolation are able to reduce the area of skin ulceration following exposure to heat and mustard gas. The specification also discloses derivates and analogs of the active peptides found in the skin extract. For example, N-methylated analogs of SEQ ID NO:1, SEQ ID NOs: 5-8, can reduce the ulceration rate following mustard gas exposure. In addition, SEQ ID NO: 5, along with SEQ ID NOs: 1, and 2, cause a reduction in ear swelling following mustard gas exposure. Finally, SEQ ID NO:12, which shares some homology with SEQ I NO:1 can reduce ear swelling following mustard gas exposure when combined with specific anti-inflammatory agents.

12. The prior art does not disclose the use of skin extracts obtained from guinea pigs following a burn and iodine exposure for the protection against inflammatory processes and noxious stimuli. The prior art includes limited examples of the claimed isolated active ingredients and their uses: the histone h2a peptide fragment LRKGNYAERVGAGAP has been used in the treatment of systemic lupus erythematosus (Datta *et al.*, USPN 6,468,537), while Fibrinopeptide A has been shown

to prevent excessive allergic reaction (Masuda & Sugiyama, *Peptides*, **2001**, *22*, 1511), have anti-inflammatory properties (Sherer *et* al., Clin. *Exp. Immunol.*, **1980**, *40*, 49) and be useful in the treatment of tumors (Staton *et al.*, US 2004/0039157). Inflammatory processes and noxious stimuli as claimed encompass an extremely wide range of disease states, conditions and environmental factors and insults. Given the relative lack of skill in the art on the use of the claimed compositions and the breadth of the claims, the burden on Applicant to describe the make and use of the skin extract and the skin extract comprising peptides and specifically peptides with SEQ ID NOs: 1, 2, 4-8 and 10-14, their homologs, analogs and derivatives, in detail is high.

13. A method for making the skin extract from guinea pigs exposed to a burn and iodine solution is disclosed. However, variability in the conditions of the extraction and burn-response of the animal could result in compositions with different components and activities. Although the specification identifies SEQ ID NOs:1-4 as active ingredients in the extract, it does not provide evidence that other peptides are present in the skin extract. Despite this, claims 1, 3-5, 7, 8, and 14-26 are drawn to skin extracts comprising an unlimited number and type of active ingredients, claims 2, 6, 9, 11, 13, 27, and 29-33 are drawn to skin extracts comprising peptides, and claims 10, 12, 28, 34 and 35 are drawn to skin extracts comprising one or more peptides from the group consisting of SEQ ID NOs: 1, 2, 4-8 and 10-14. It is not clear from the specification if peptides of SEQ ID NOs: 5-8 and 10-14, their homologs, analogs and derivatives, or additional unidentified peptides or molecules are to be synthesized or isolated and then added to the skin extract, or if they are obtained from the disclosed extraction

procedure. The detailed structure of other peptides and compounds included in the scope of the claims are not described. As stated above, specific examples for the use of these compositions are given only for protection from thermal burns and exposure to mustard gas. Amongst the peptides tested there is significant variation in effectiveness with two peptides, the $MeGly^2/MeAla^5/MeILeu^8$ analog of SEQ ID NO:1 and SEQ ID NO: 12, having no effect in isolation in assays involving mustard gas exposure. Therefore, it is impossible to predict that all peptides found in the skin extract or related to the peptides found in the skin extract would be useful for protecting against exposure to mustard gas. Lacking a full chemical characterization and more detailed information on the chemical and structural properties that give rise to the claimed function, it would be difficult to reproducibly make the skin extract or the relevant active ingredients as claimed. Significant experimentation would be required to first identify the active compounds and then make them.

14. Regarding the other inflammatory processes and noxious stimuli included in the scope of claims 1-35, no data is presented. The state of the art at the time the invention was made suggests that there is significant unpredictability associated with treating such conditions. For example, Citron teaches that current drugs for Alzheimer's disease are safe but of limited benefit to most patents and that the use of anti-inflammatory drugs is promising but in the developmental stages for this disease (*Nat. Neurosci.*, **2002**, *5*, 1055). Rizzello *et al.* teach that Crohn's disease patients are commonly refractive to conventional therapy (*Ailmet Pharmacol. Ther.*, **2002**, *16*, 40). Korczyn & Nussbaum teach that there is a lack of consensus on how to treat Parkinson's disease

during its various stages (*Drugs*, **2002**, *62*, 775). Shuk *et al.* teach that treatments to present disability and death from muscular dystrophy are non-existent (*Curr. Op. Neur.*, **2002**, *15*, 563). Coussens & Werb teach that inflammation is a critical component of tumor progression but that related therapies are only in the developmental stage (*Nature*, **420**, *420*, 860). Wiendl & Hohlfeld teach that despite promising results from animal models and phase I/II studies, many drugs and strategies have failed to successfully treat multiple sclerosis (*Biodrug*, **2002**, *16*, 183). Finally, Ashcroft *et al.* teach that there is substantial variability between and within patients over the course of psoriasis (*J. Clin. Pharm. & Ther.*, **2000**, *25*, 1). Given the state of the art at the time the invention was made, one of ordinary skill in the art would not reasonably have been able to predict which of the claimed species, if any, would be useful for treating all diseases and conditions covered by the scope of the claim.

15. Given the limited disclosure of working examples, the state of the art on the use of skin extracts, the active ingredients found in skin extracts and peptides with SEQ ID NOs: 1, 2, 4-8 and 10-14, the lack of predictability associated with treating inflammatory processes, and the breadth of the claims, there would be an undue burden on one attempting to make or use the invention as claimed. In view of all of these factors, the specification is enabling for the make and use of skin extracts for protecting against inflammatory processes and noxious stimuli.

16. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

17. Claims 11, 12, 29 and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

18. The term "plurality" in claims 11, 12, 29 and 35 is a relative term which renders the claim indefinite. The term "plurality" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The number and identity of the peptides included in the skin extract is rendered indefinite by the use of the term "plurality".

Claim Rejections - 35 USC § 102

19. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.
>
> The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

20. Claims 1-5, 7-12, 16-30 and 32-35 are rejected under 35 U.S.C. 102(a) as being anticipated by Masuda & Sugiyama (*Peptides*, **2001**, *22*, 1511). Masuda & Sugiyama teach that the administration of fibrinopeptide A (ADSGEGDFLAEGGGV) to mice can reduce excessive allergic reaction (see abstract). This peptide is identical to SEQ ID NO: 9 of the instant application, and is an analog of SEQ ID NOs: 2 and 4, and a homolog of SEQ ID NO: 11.

21. Claims 1-5, 7-12, 16-30 and 32-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Scherer *et al.* (*Clin. Exp. Immunol.*, **1980**, *40*, 49). Scherer *et al.* teach the administration of fibrinopeptide A to treat experimental allergic encephalomyelitis (see abstract). Scherer *et al.* teach that fibrinopeptide A has anti-inflammatory properties (see page 59). This peptide is identical to SEQ ID NO: 9 of the instant application, and is an analog of SEQ ID NOs: 2 and 4, and a homolog of SEQ ID NO: 11.

22. Claims 1-5, 7-12, 16-30 and 32-35 are rejected under 35 U.S.C. 102(e) as being anticipated by Datta *et al.* (USPN 6,468,537). Datta *et al.* teach pharmaceutical compositions comprising histone h2a peptide fragments including the sequence LRKGNYAERVGAGAP (see Figure 17A ,column 2, lines 46-52, and column 2, line 66 through column 3, line 3). This peptide is an analog of SEQ ID NO:12, and a homolog of SEQ ID NOs: 1 and 10 of the instant application. SEQ ID NOs: 5-8 of the instant application are derivatives of the peptide taught by Datta *et al.* In addition, Datta *et al.*

teach the administration of these peptides for the treatment of systemic lupus erthematosus (see column 4, lines 19-30).

23. Claims 1-5, 7-12, 16-30 and 32-35 are rejected under 35 U.S.C. 102(e) as being anticipated by Staton *et al.* (US 2004/0039157 A1). Staton *et al.* teach the administration of peptide ADSGEGDFLAEGGGVRGPRVVEHR (see Figure 5B) for the treatment of tumors (see paragraphs 0125-0133). This peptide is a homolog and/or analog of the fibrinopeptide A peptides in the instant application, specifically SEQ ID NOs, 2, 4, 9 and 11.

24. In each the four rejections made under 35 U.S.C. 102 outlined above, the references do not teach that the peptides are part of a skin extract. Since Applicants are claiming a pharmaceutical product and methods of for its use, this is immaterial to either. The isolation of the active ingredients does not affect the structure of the component itself. The identical chemical structure could be obtained by other means such as chemical synthesis. "Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a

different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. In re Marosi, 218 USPQ 289, 292 (Fed. Cir. 1983).

Conclusion

25. No claims are allowed.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Bradley whose telephone number is (571) 272-9044. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

27. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

28. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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